Supporting Information for

Synthesis of Heterocyclic (Triazole, Furoxan, Furazan) Fused Pyridazine Di-*N*-Oxides via Hypervalent Iodine Oxidation

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Contents

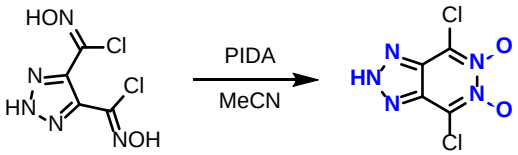
I. General information

All reagents were purchased from commercial sources (Energy Chemical, Adamas-beta®, J&K Scientific, Sigma-Aldrich) and used without purification unless otherwise mentioned. The products were purified by column chromatography over silica gel (200-300 size). ^{1}H and ^{13}C Nuclear Magnetic Resonance (NMR) spectra were recorded at 25 °C on a Bruker 400 MHz, 100 MHz, and TMS was used as internal standard. Infrared spectra (IR) were obtained on a PerkinElmer Spectrum BX FT-IR instrument equipped with an ATR unit at 25 °C. Elemental analyses of C/H/N were investigated on a Vario EL III Analyzer. High resolution mass spectra (HRMS) were recorded on Thermo Scientific LTQ Orbitrap XL and Thermo Scientific Q Exactive by using ESI method. The onset decomposition temperature was recorded on TA Discovery DSC 25.

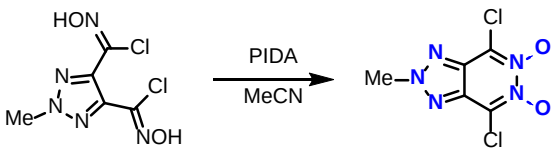
Note of Caution:

Furoxan and azide compounds are explosive substance and may explode under certain conditions. Appropriate safety precautions should be taken when preparing and handling.

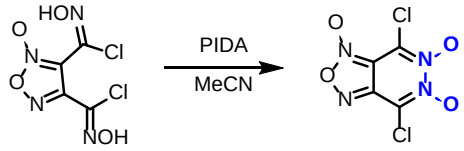
II. Experimental procedure



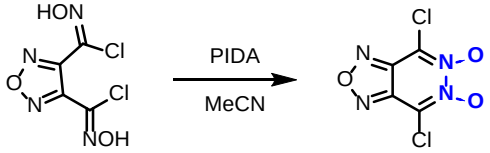
General procedure for the synthesis of triazole-fused pyradizine di-*N*-dioxide: In a Schlenk tube, a solution of 1,4-dioxime (2.0 mmol, 1.0 equiv), PIDA (2.4 mmol, 1.2 equiv) in acetonitrile (2 mL) was stirred for 1 h at 25 °C. Then white solid was filtered, washed with petroleum ether (5 mL) and air dried to give triazole-fused pyradizine di-*N*-dioxide.



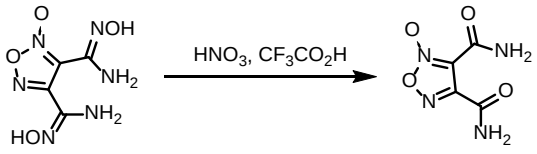
In a Schlenk tube, a solution of 1,4-dioxime (2.0 mmol, 1.0 equiv), PIDA (2.4 mmol, 1.2 equiv) in acetonitrile (2 mL) was stirred for 1 h at 25 °C. Then saturated aq $NaHCO_3$ solution is added and extracted with EA (3 × 10 mL). Combined organic layers was dried over Na_2SO_4 and filtered, evacuated under vacuum. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 4/1) to give triazole-fused pyradizine di-*N*-dioxide.



General procedure for the synthesis of furoxan-fused pyradizine di-*N*-dioxide: In a Schlenk tube, a solution of 1,4-dioxime (0.5 mmol, 1.0 equiv), PIDA (0.6 mmol, 1.2 equiv) in acetonitrile (2 mL) was stirred for 30 min at 25 °C. Then saturated aq $NaHCO_3$ solution is added and extracted with EA (3 × 10 mL). Combined organic layers was dried over Na_2SO_4 and filtered, evacuated under vacuum. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1) to give furoxan-fused pyradizine di-*N*-dioxide.

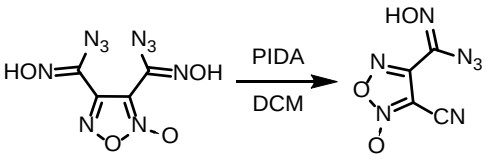


General procedure for the synthesis of furazan-fused pyradizine di-*N*-dioxide: In a Schlenk tube, a solution of 1,4-dioxime (0.5 mmol, 1.0 equiv), PIDA (0.6 mmol, 1.2 equiv) in acetonitrile (2 mL) was stirred for 30 min at 25 °C. Then saturated aq $NaHCO_3$ solution is added and extracted with EA (3 × 10 mL). Combined organic layers was dried over Na_2SO_4 and filtered, evacuated under vacuum. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1) to give furazan-fused pyradizine di-*N*-dioxide.



General procedure for the synthesis of 3,4-dicarbamoyl-1,2,5-oxadiazole 2-oxide: In a Schlenk tube, 1,4-dioxime (1.0 mmol, 1.0 equiv) was added at -20 °C to a mixture of HNO_3 (d = 1.495 g/cm^3,

1.0 mL, 23.7 mmol) and CF_3CO_2H (d = 1.489 g/cm^3, 2.0 mL, 26.1 mmol). The reaction mixture was stirred for 10 min at this temperature, poured into crushed ice (10 g). The precipitate was filtered, washed with water and dried.



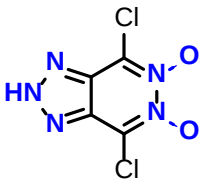
General procedure for the synthesis of 4-(azido(hydroxyimino)methyl)-3-cyano-1,2,5-oxadiazole 2-oxide: To a solution of 1,4-dioxime (0.5 mmol, 1.0 equiv) in DCM (5 mL), PIDA (0.6 mmol, 1.2 equiv) was added in portion, then the mixture was stirred for 30 min at 25 °C. Saturated aq $NaHCO_3$ solution is added and extracted with DCM (3 × 10 mL). Combined organic layers was dried over Na_2SO_4 and filtered, evacuated under vacuum. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10/1) to give 4-(azido(hydroxyimino)methyl)-3-cyano-1,2,5-oxadiazole 2-oxide.

III. X-Ray crystallographic data

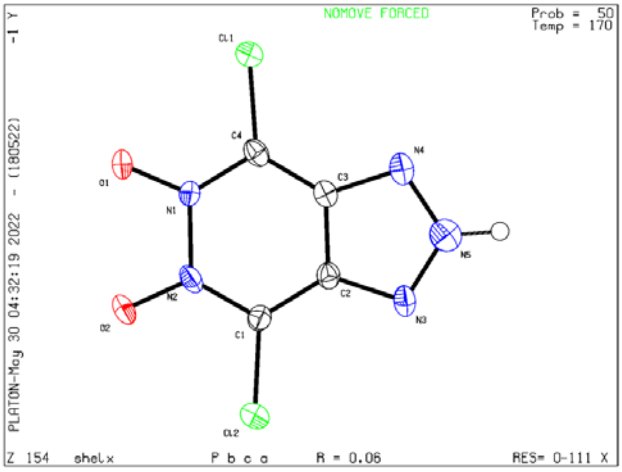
Crystal Structure of

4,7-dichloro-2H-[1,2,3]triazolo[4,5-d]pyridazine 5,6-dioxide (4)

(CCDC No. **2175705**)



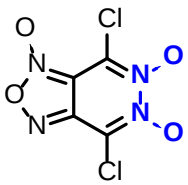
Empirical formula	$C_4HCl_2N_5O_2$
Temperature	170.0 K
Wavelength	0.71073 Å
Unit cell dimensions	a = 13.829(3) Å b = 7.0389(13) Å c = 15.224(3) Å alpha = 90 deg. beta = 90 deg.

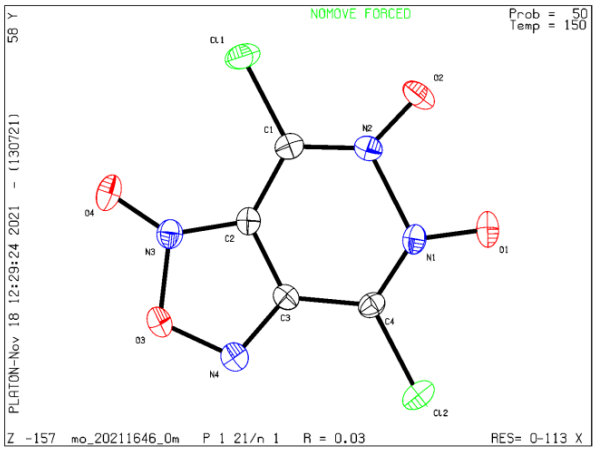
	gamma = 90 deg.
Volume	1482.0 (5) $Å^3$
Z	8
Calculated density	1.990 g/cm^3
Absorption coefficient	0.845 mm^{-1}
F(000)	880.0
Crystal size	0.12 x 0.08 x 0.05 mm
Θ range for data collection	2.676 to 26.376 deg.
Reflections collected / unique	4614 / 1485[R(int) = 0.0795]
Data / restraints / parameters	1485 / 4 / 121
Goodness-of-fit on F^2	1.048
Final R indices [I>2sigma(I)]	R1 = 0.0622, wR2 = 0.1485
Rindices (all data)	R1 = 0.1028, wR2 = 0.1733
	
Growth in DMF/DCM at room temperature	

Crystal Structure of

4,7-dichloro-[1,2,5]oxadiazolo[3,4-d]pyridazine 1,5,6-trioxide (8)

(CCDC No. **2175700**)

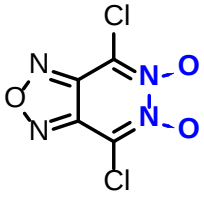


Empirical formula	$C_4Cl_2N_4O_4$
Temperature	150.0 K
Wavelength	0.71073 Å
Unit cell dimensions	a = 9.1210(7) Å b = 5.9953(5) Å c = 14.5570(12) Å alpha = 90 deg. beta = 100.853(3) deg. gamma = 90 deg.
Volume	781.78 (11) $Å^3$
Z	4
Calculated density	2.030 g/cm^3
Absorption coefficient	0.824 mm^{-1}
F(000)	472.0
Crystal size	0.13 x 0.06 x 0.03 mm
2Θ range for data collection	4.89 to 52.816 deg.
Reflections collected / unique	8446 / 1604 [R(int) = 0.0412]
Data / restraints / parameters	1604 / 1 / 127
Goodness-of-fit on F^2	1.076
Final R indices [I>2sigma(I)]	R1 = 0.0312, wR2 = 0.0602
Rindices (all data)	R1 = 0.0470, wR2 = 0.0681
	
Growth in EA/PE at room temperature	

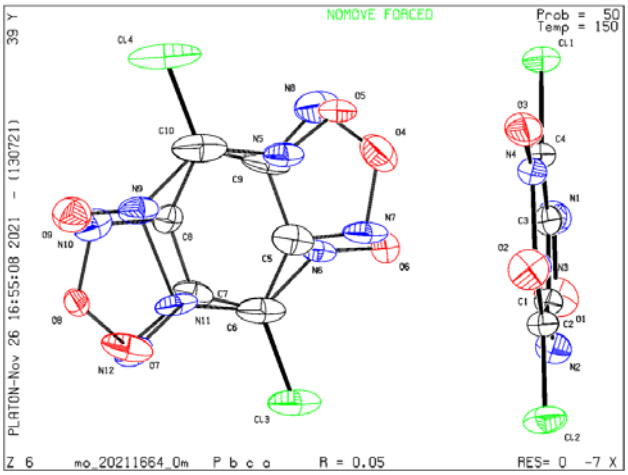
Crystal Structure of

4,7-dichloro-[1,2,5]oxadiazolo[3,4-d]pyridazine 5,6-dioxide (12)

(CCDC No. **2175701**)



Empirical formula	$C_4Cl_2N_4O_3$
Temperature	150.0 K
Wavelength	0.71073 Å
Unit cell dimensions	a = 8.9927(5) Å b = 15.7743(9) Å c = 21.8858(14) Å alpha = 90 deg. beta = 90 deg. gamma = 90 deg.
Volume	3104.6(3) $Å^3$
Z	16
Calculated density	1.908 g/cm^3
Absorption coefficient	0.813 mm^{-1}
F(000)	1760.0
Crystal size	0.12 x 0.08 x 0.05 mm
2Θ range for data collection	5.49 to 52.862 deg.
Reflections collected / unique	26541 / 3177 [R(int) = 0.0511]
Data / restraints / parameters	3177 / 581 / 316
Goodness-of-fit on F^2	1.026
Final R indices [I>2sigma(I)]	R1 = 0.0537, wR2 = 0.1241
Rindices (all data)	R1 = 0.0728, wR2 = 0.1391

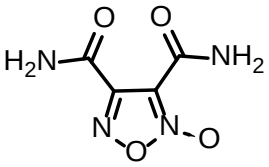


Growth in EA/PE at room temperature

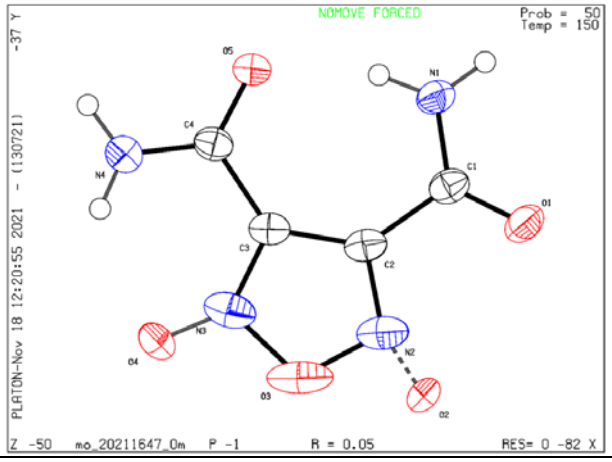
Crystal Structure of

3,4-dicarbamoyl-1,2,5-oxadiazole 2-oxide (14)

(CCDC No. **2175706**)



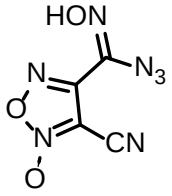
Empirical formula	$C_4H_4N_4O_4$
Temperature	150.0 K
Wavelength	0.71073 Å
Unit cell dimensions	a = 5.0887(16) Å b = 7.8054(19) Å c = 7.906(2) Å alpha = 89.639(7) deg. beta = 80.847(10) deg. gamma = 89.131(10) deg.
Volume	309.99(15) $Å^3$
Z	2
Calculated density	1.844 g/cm^3
Absorption coefficient	0.166 mm^{-1}

F(000)	176.0
Crystal size	0.12 x 0.05 x 0.03 mm
2Θ range for data collection	5.218 to 52.696 deg.
Reflections collected / unique	3278 / 1239 [R(int) = 0.0373]
Data / restraints / parameters	1239 / 7 / 134
Goodness-of-fit on F^2	1.078
Final R indices [I>2sigma(I)]	R1 = 0.0508, wR2 = 0.1044
Rindices (all data)	R1 = 0.0753, wR2 = 0.1182
	
Growth in DMF/Et_2O/DCM at room temperature	

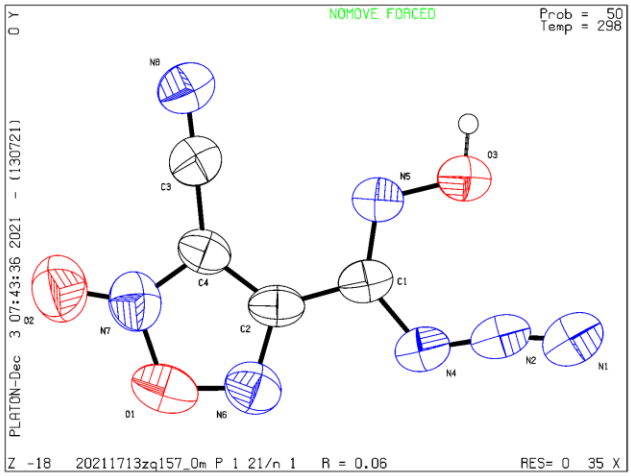
Crystal Structure of

4-(azido(hydroxyimino)methyl)-3-cyano-1,2,5-oxadiazole 2-oxide (16)

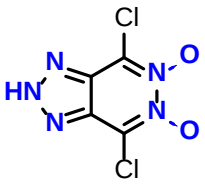
(CCDC No. **2175709**)



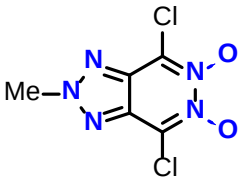
Empirical formula	$C_4HN_7O_3$
Temperature	298.0 K
Wavelength	0.71073 Å
Unit cell dimensions	a = 9.3585(14) Å b = 5.3944(9) Å

	c = 15.367(2) Å alpha = 90 deg. beta = 94.035(4) deg. gamma = 90 deg.
Volume	773.8(2) $Å^3$
Z	4
Calculated density	1.675 g/cm^3
Absorption coefficient	0.145 mm^{-1}
F(000)	392.0
Crystal size	0.12 x 0.08 x 0.05 mm
2Θ range for data collection	4.946 to 52.874 deg.
Reflections collected / unique	5321 / 1582 [R(int) = 0.0449]
Data / restraints / parameters	1582 / 1 / 131
Goodness-of-fit on F^2	1.031
Final R indices [I>2sigma(I)]	R1 = 0.0584, wR2 = 0.1328
Rindices (all data)	R1 = 0.1176, wR2 = 0.1638
	
Growth in EA/PE at room temperature	

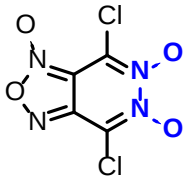
IV. Characterization data for the products



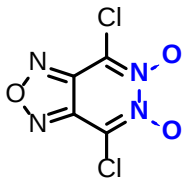
4,7-Dichloro-2*H*-[1,2,3]triazolo[4,5-d]pyridazine 5,6-dioxide (4) This compound was prepared according to the general procedure for the synthesis of triazole-fused pyradizine di-*N*-dioxide, yield 0.37 g (85%). White solid; T_{dec}: 190.7 ℃; **^{1}H NMR** (400 MHz, DMSO) δ 16.48 (s, 1H). **^{13}C NMR** (100 MHz, DMSO) δ 131.8, 115.9. **IR** (cm^{-1}) 2999, 2949, 1782, 1608, 1510, 1309, 1191, 1128, 977, 941, 907, 784, 693, 525. **Elemental analysis** (%) for $C_4HCl_2N_5O_2$ (221.99): calcd: C 21.64, H 0.45, N 31.55. Found: C 21.17, H 0.64, N 31.76.



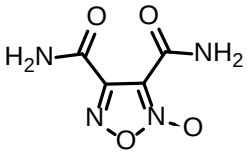
4,7-Dichloro-2-methyl-2H-[1,2,3]triazolo[4,5-d]pyridazine 5,6-dioxide (4a) This compound was prepared according to the general procedure for the synthesis of triazole-fused pyradizine di-*N*-dioxide, yield 0.37 g (78%). Yellow solid; T_{dec}: 170.2 ℃; **^{1}H NMR** (400 MHz, DMSO) δ 4.49 (s, 3H). **^{13}C NMR** (100 MHz, DMSO) δ 133.7, 115.7, 44.2. **Elemental analysis** (%) for $C_4HCl_2N_5O_2$ (236.01): calcd: C 25.45, H 1.28, N 29.67. Found: C 25.07, H 1.21, N 30.02.



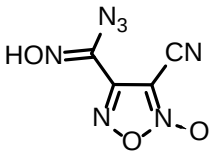
4,7-Dichloro-[1,2,5]oxadiazolo[3,4-d]pyridazine 1,5,6-trioxide (8) This compound was prepared according to the general procedure for the synthesis of furoxan-fused pyradizine di-*N*-dioxide. Purified on silica gel chromatography to give the product (89.6 mg, 75%) (petroleum ether/ethyl acetate = 10/1). Yellow solid; T_{dec}: 109.6 ℃; **^{13}C NMR** (100 MHz, CD_3CN) δ 143.8, 110.0, 107.8, 105.8. **IR** (cm^{-1}) 1605, 1504, 1396, 1255, 1185, 1078, 977, 910, 812, 747, 687, 473. **Elemental analysis** (%) for $C_4Cl_2N_4O_4$ (238.97): calcd: C 20.10, N 23.45. Found: C 19.70, N 23.97.



4,7-Dichloro-[1,2,5]oxadiazolo[3,4-d]pyridazine 5,6-dioxide (12) This compound was prepared according to the general procedure for the synthesis of furazan-fused pyradizine di-*N*-dioxide. Purified on silica gel chromatography to give the product (80.2 mg, 72%) (petroleum ether/ethyl acetate = 10/1). Yellow solid; T_{dec}: 135.8 °C; **^{13}C NMR** (100 MHz, CD_3CN) δ 143.1, 108.8. **IR** (cm^{-1}) 1634, 1522, 1358, 1235, 985, 930, 877, 860, 743, 690, 589, 538, 433. **Elemental analysis** (%) for $C_4Cl_2N_4O_3$ (222.97): calcd: C 21.55, N 25.13. Found: C 21.83, N 24.64.



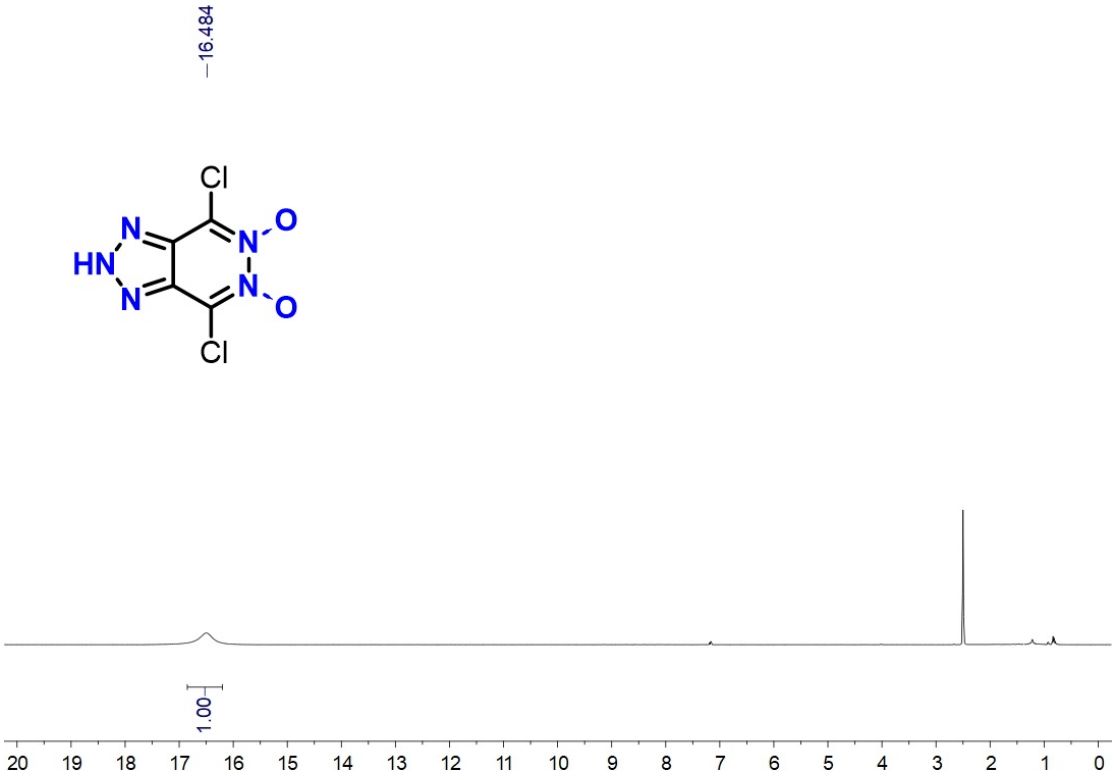
3,4-Dicarbamoyl-1,2,5-oxadiazole 2-oxide (14) Light yellow solid, 51.6 mg (31%); T_{dec}: 245.6°C; **^{1}H NMR** (400 MHz, DMSO) δ 8.71 (s, 1H), 8.42 (s, 1H), 8.35 (s, 1H), 8.30 (s, 1H). **^{13}C NMR** (100 MHz, DMSO) δ 158.4, 155.7, 152.0, 110.6. **HRMS** (ESI) m/z calcd for $C_4H_4N_4NaO_4^+$ $(M+Na)^+$ 195.01248, found 195.01263.



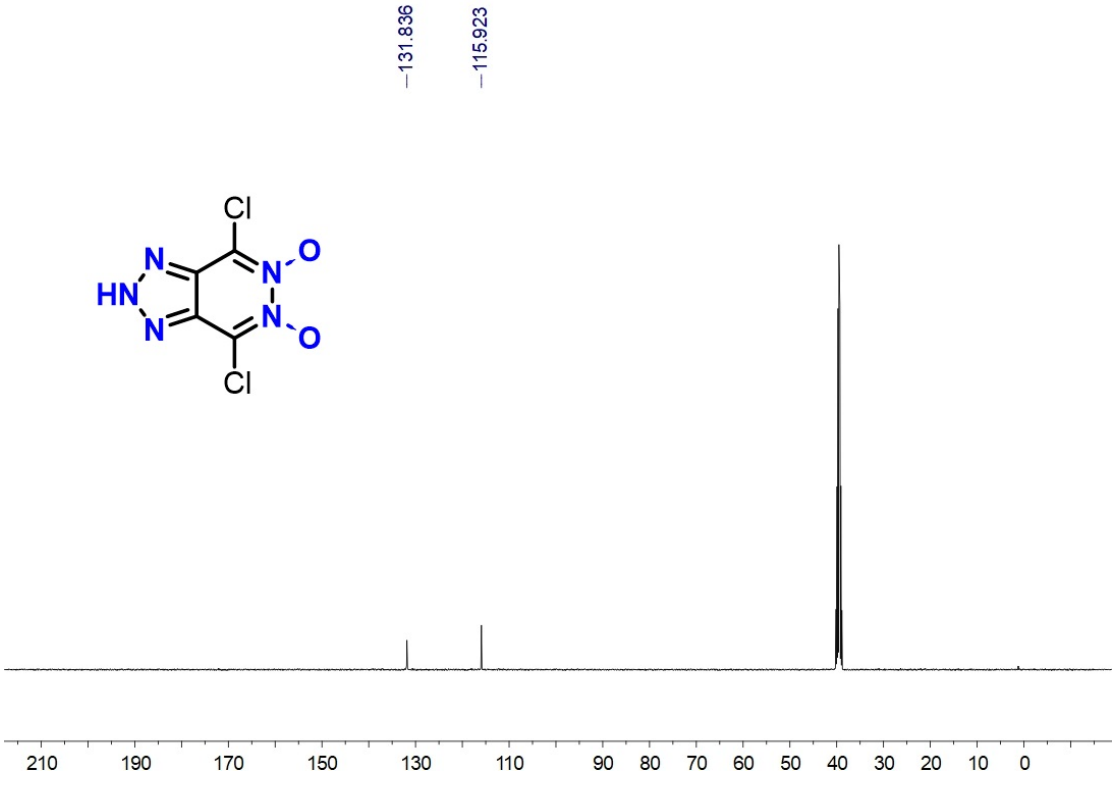
4-(Azido(hydroxyimino)methyl)-3-cyano-1,2,5-oxadiazole 2-oxide (16) White solid, 58.5 mg (60%); T_{dec}: 130.9 °C; **^{1}H NMR** (400 MHz, Acetone-d_6) δ 12.22 (s, 1H). **^{13}C NMR** (100 MHz, Acetone-d_6) δ 149.6, 134.9, 106.7, 96.9. **IR** (cm^{-1}) 3323, 2161, 2112, 1621, 1603, 1475, 1405, 1337, 1262, 1037, 1015, 945, 863, 823, 694, 522, 441. **Elemental analysis** (%) for $C_4HN_7O_3$ (195.10): calcd: C 24.63, H 0.52, N 50.26. Found: C 24.20, H 0.61, N 50.68.

V. Figures of ^{1}H-NMR, ^{13}C-NMR spectra

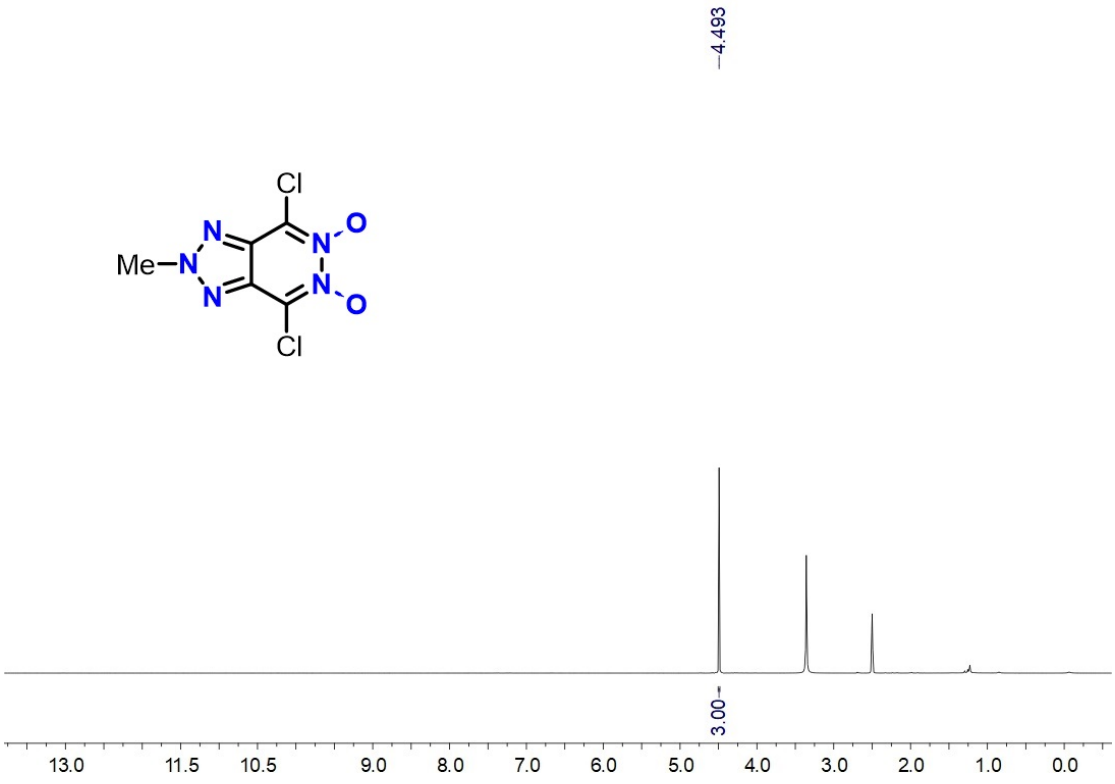
^{1}H NMR Spectrum of **4** (DMSO, 400 MHz)



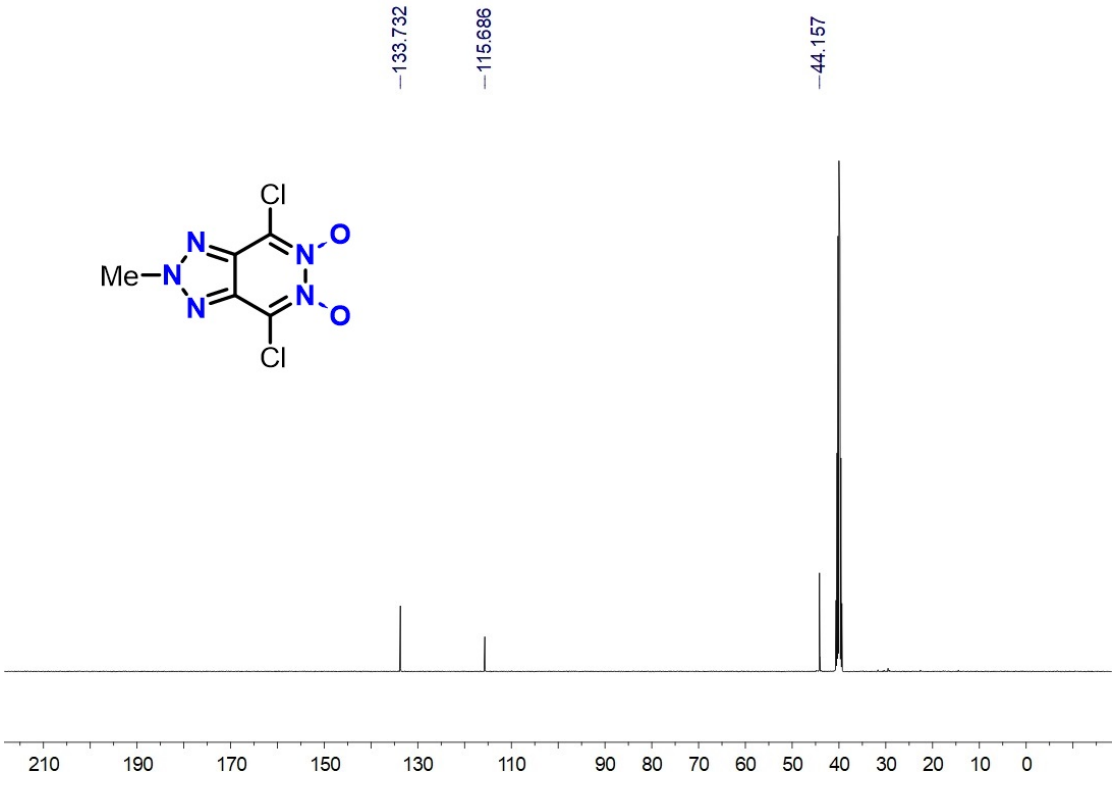
^{13}C NMR Spectrum of **4** (DMSO, 100 MHz)



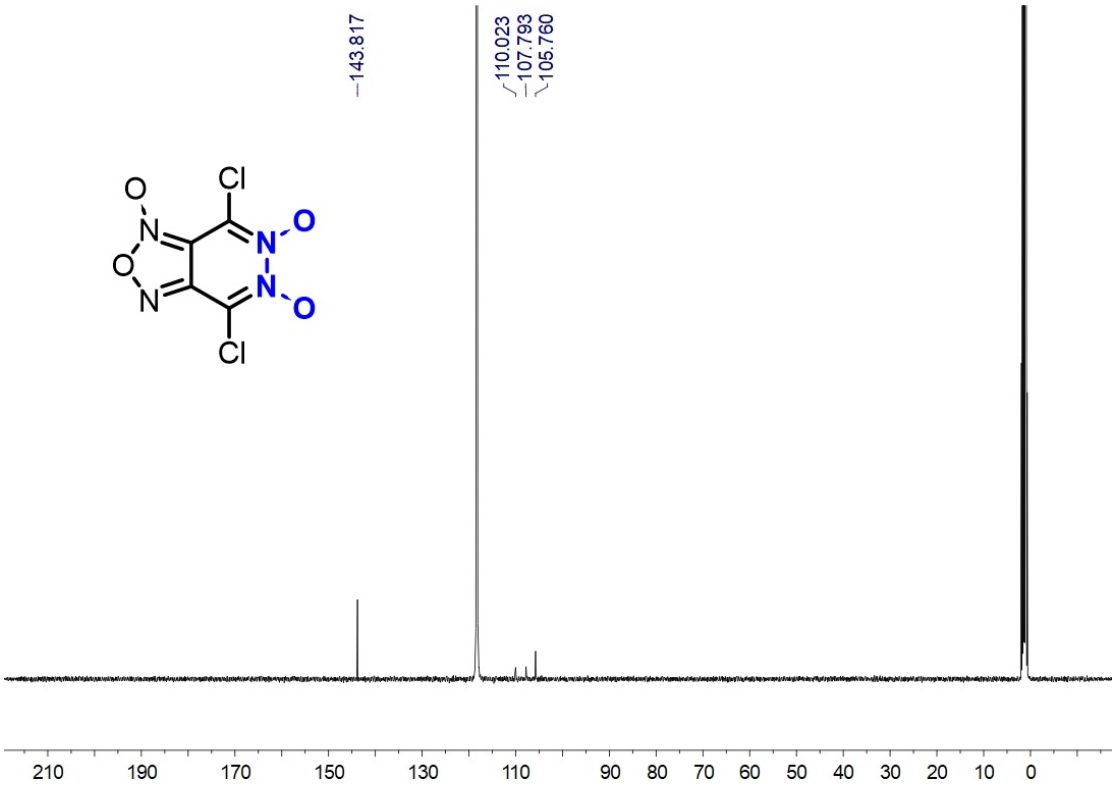
^{1}H NMR Spectrum of **4a** (DMSO, 400 MHz)



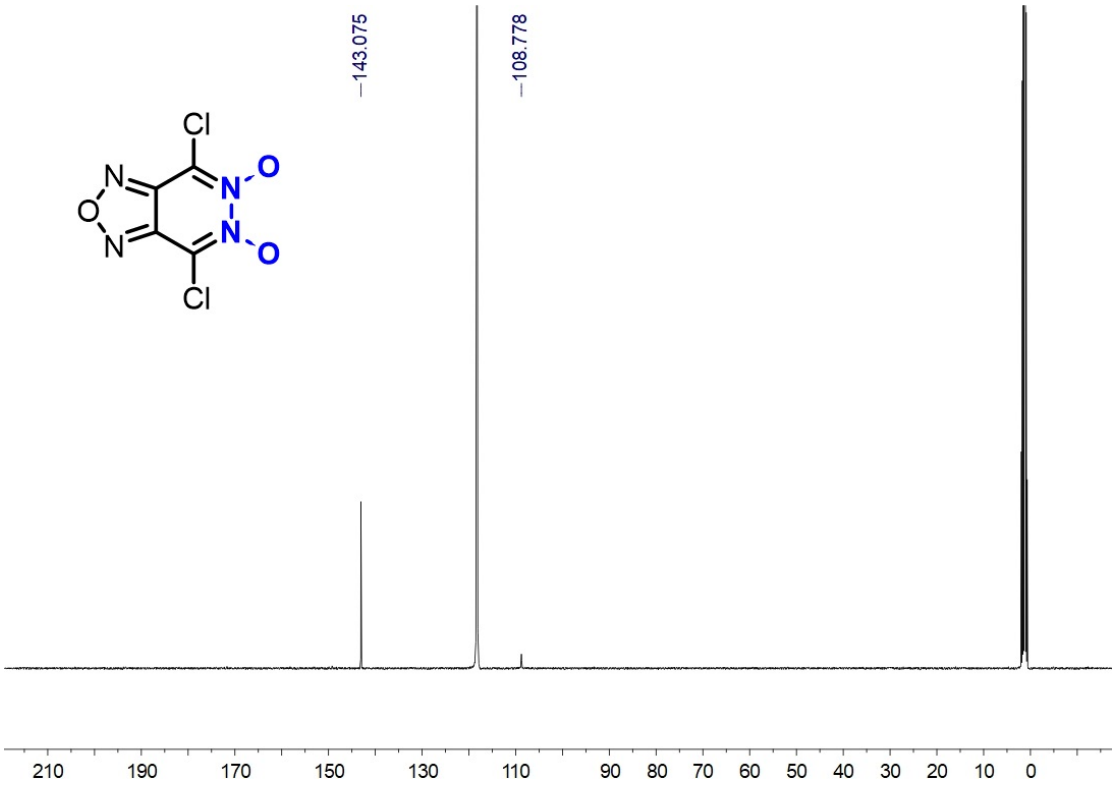
^{13}C NMR Spectrum of **4a** (DMSO, 100 MHz)



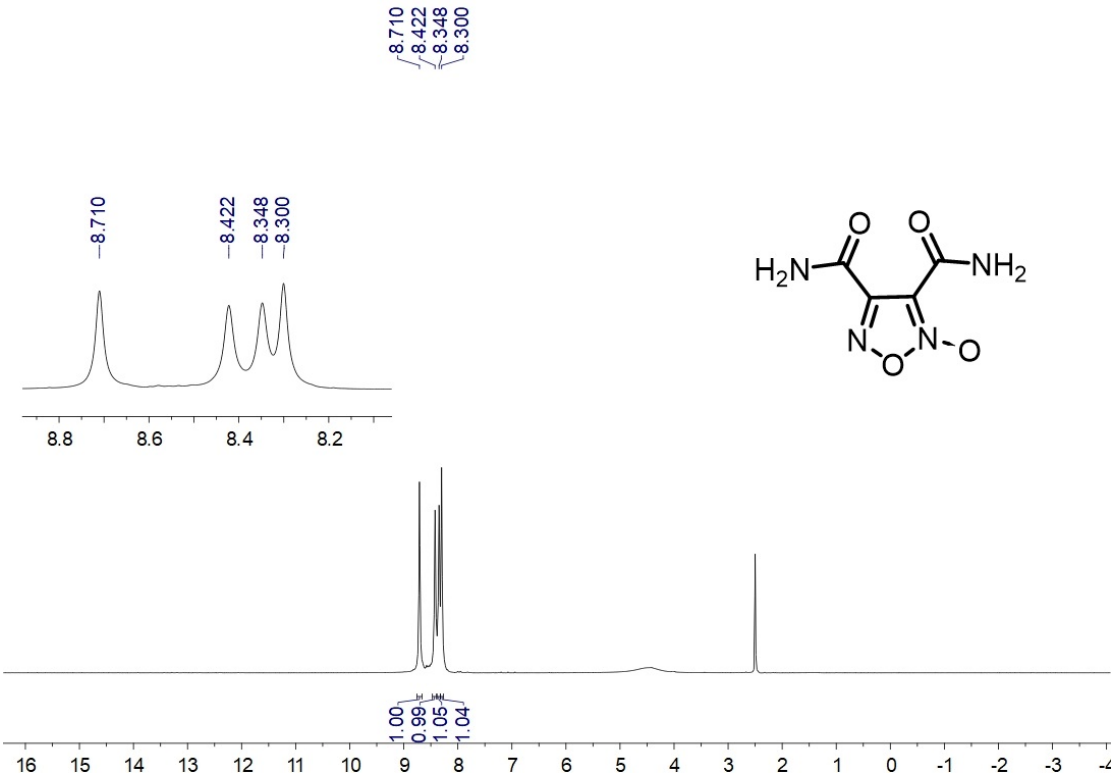
^{13}C NMR Spectrum of **8** (CD_3CN, 100 MHz)



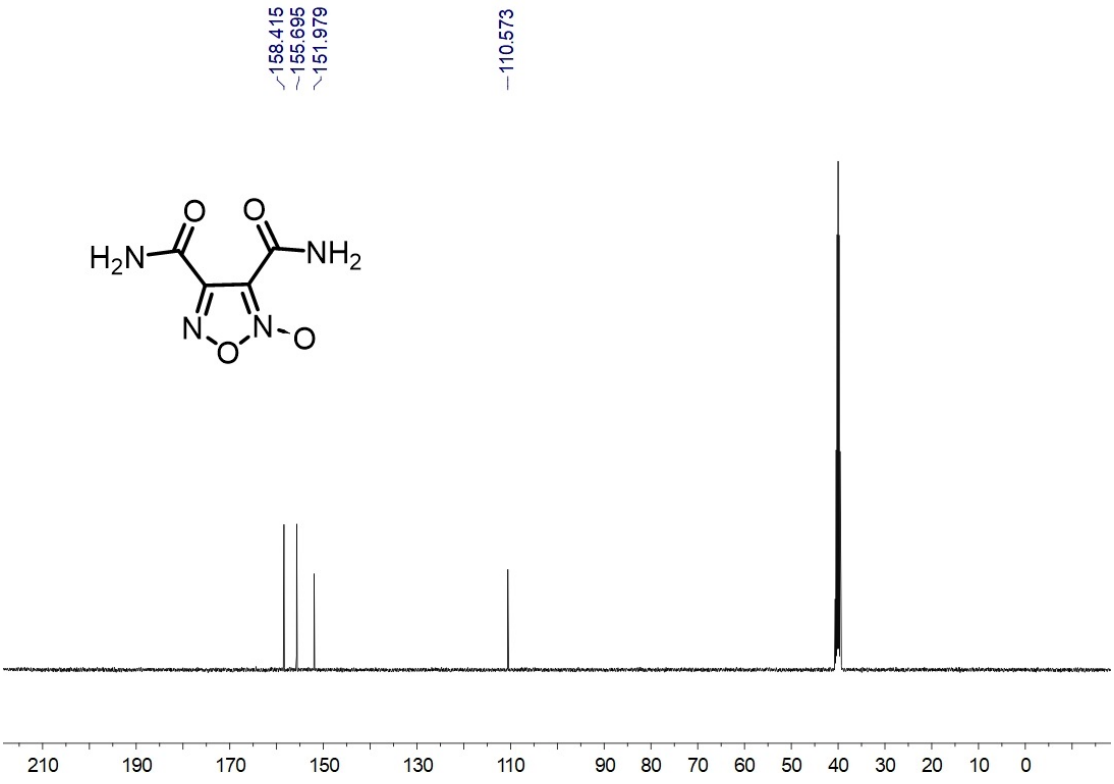
^{13}C NMR Spectrum of **12** (CD_3CN, 100 MHz)



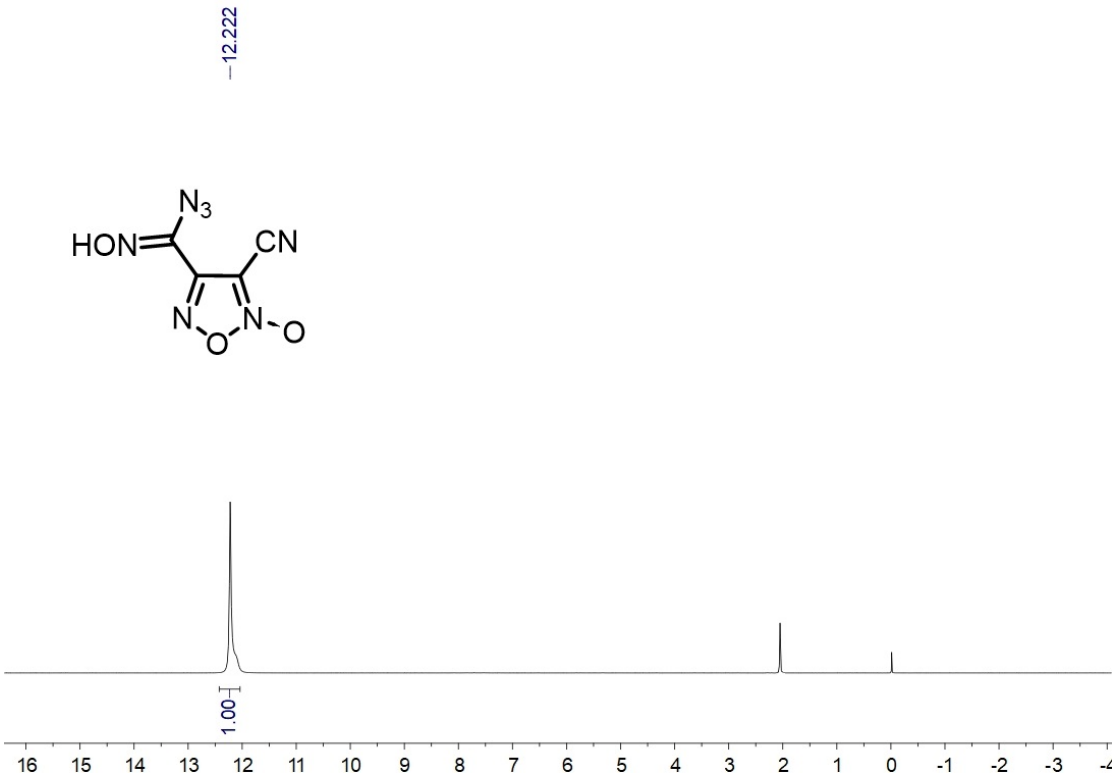
^{1}H NMR Spectrum of **14** (DMSO, 400 MHz)



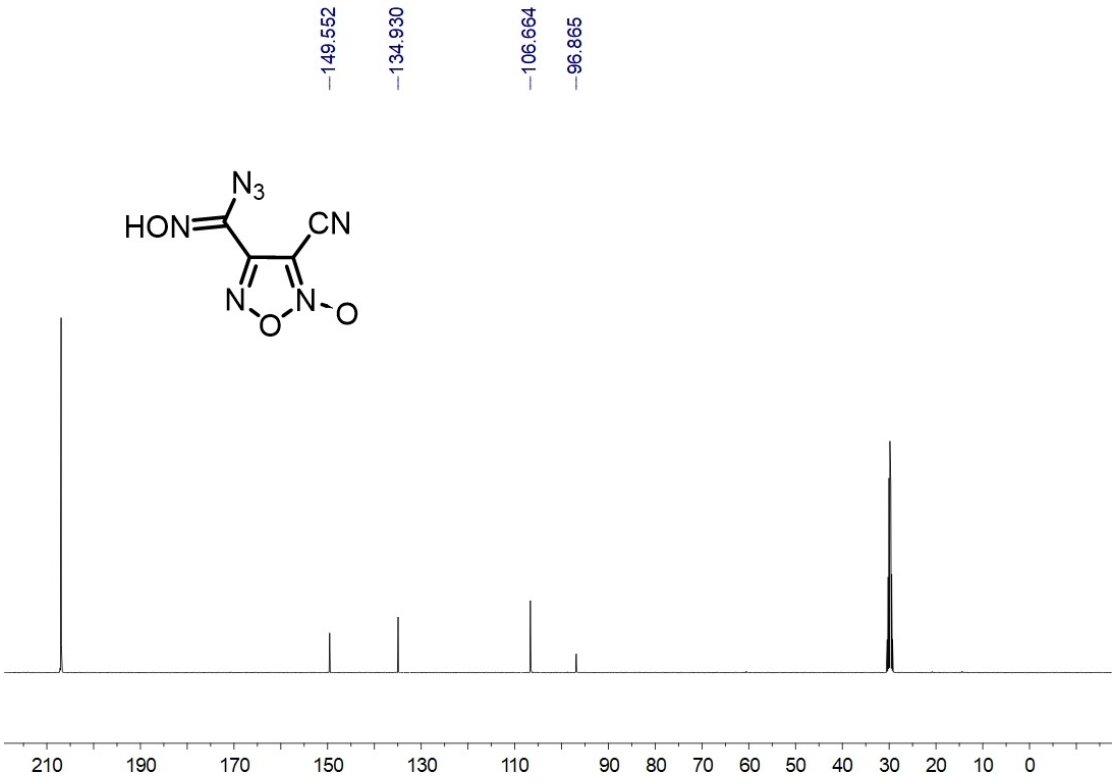
^{13}C NMR Spectrum of **14** (DMSO, 100 MHz)



^{1}H NMR Spectrum of **16** (Acetone-d_6, 400 MHz)

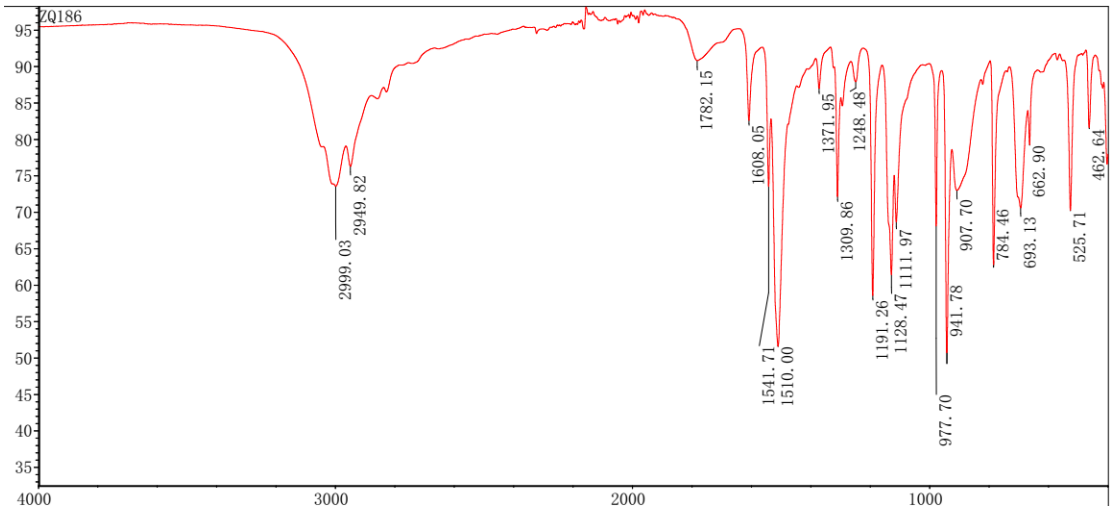


^{13}C NMR Spectrum of **16** (Acetone-d_6, 100 MHz)

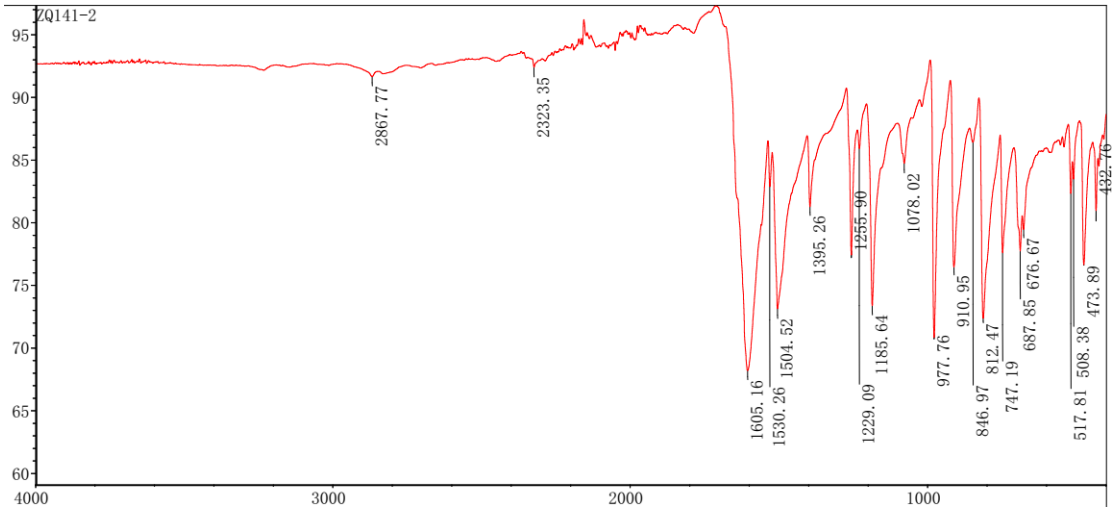


VI. IR spectra

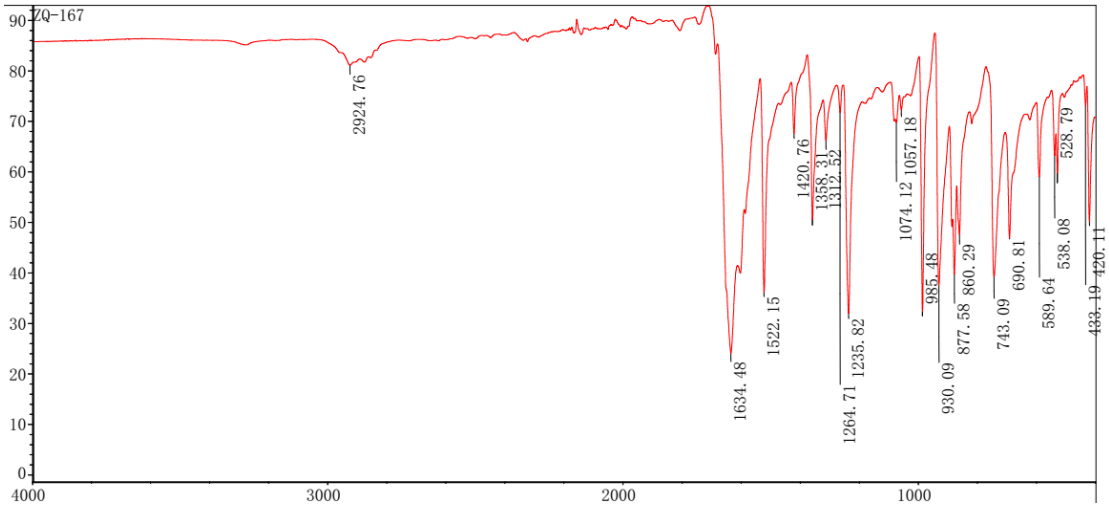
IR spectrum of compound **4**



IR spectrum of compound **8**



IR spectrum of compound **12**



IR spectrum of compound **16**